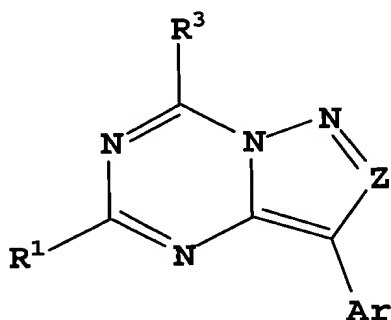
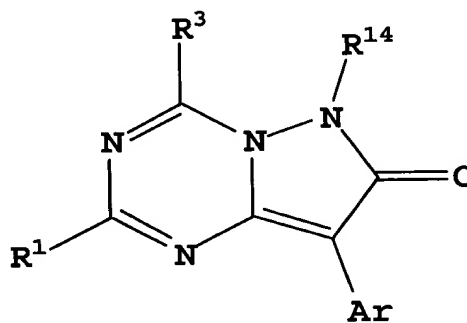


B<sup>1</sup> 1. A method of treating a disorder induced or facilitated by CRF in a mammal comprising administering to said mammal a therapeutically effective amount of a compound of Formulae (1) or (2):



(1)



(2)

isomers thereof, stereoisomeric forms thereof, mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt forms thereof, wherein:

Z is CR<sup>2</sup>;

Ar is selected from phenyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, furanyl, thienyl, benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each Ar optionally substituted with 1 to 5 R<sup>4</sup> groups and each Ar is attached to an unsaturated carbon atom;

R<sup>1</sup> is independently selected at each occurrence from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>2</sub>-C<sub>4</sub> alkynyl, halo, CN, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>12</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>12</sub> alkoxyalkyl, C<sub>2</sub>-C<sub>10</sub> cyanoalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, NR<sup>9</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>4</sub> alkyl-NR<sup>9</sup>R<sup>10</sup>, NR<sup>9</sup>COR<sup>10</sup>, OR<sup>11</sup>, SH or S(O)<sub>n</sub>R<sup>12</sup>;

R<sup>2</sup> is selected from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>2</sub>-C<sub>4</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, C<sub>1</sub>-C<sub>4</sub> hydroxyalkyl, halo, CN, -NR<sup>6</sup>R<sup>7</sup>, NR<sup>9</sup>COR<sup>10</sup>, -NR<sup>6</sup>S(O)<sub>n</sub>R<sup>7</sup>, S(O)<sub>n</sub>NR<sup>6</sup>R<sup>7</sup>, C<sub>1</sub>-C<sub>4</sub> haloalkyl, -OR<sup>7</sup>, SH or -S(O)<sub>n</sub>R<sup>12</sup>;

R<sup>3</sup> is selected from:

-H, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>7</sup>, N(COR<sup>7</sup>)<sub>2</sub>,

contd.  
B<sup>1</sup>

NR<sup>8</sup>CONR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, N(OR<sup>7</sup>)R<sup>6</sup>, CONR<sup>6</sup>R<sup>7</sup>, aryl, heteroaryl and heterocycle, or  
-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>5</sub>-C<sub>8</sub> cycloalkenyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl or C<sub>6</sub>-C<sub>10</sub> cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, NR<sup>16</sup>R<sup>15</sup>, CONR<sup>16</sup>R<sup>15</sup>, aryl, heteroaryl and heterocyclyl;

R<sup>4</sup> is independently selected at each occurrence from: C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, NO<sub>2</sub>, halo, CN, C<sub>1</sub>-C<sub>4</sub> haloalkyl, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>COR<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>7</sup>, COR<sup>7</sup>, OR<sup>7</sup>, CONR<sup>6</sup>R<sup>7</sup>, CO(NOR<sup>9</sup>)R<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, or S(O)<sub>n</sub>R<sup>7</sup>, where each such C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl and C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>4</sub> alkyl, NO<sub>2</sub>, halo, CN, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>COR<sup>7</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>7</sup>, COR<sup>7</sup> OR<sup>7</sup>, CONR<sup>6</sup>R<sup>7</sup>, CO<sub>2</sub>R<sup>7</sup>, CO(NOR<sup>9</sup>)R<sup>7</sup>, or S(O)<sub>n</sub>R<sup>7</sup>;

R<sup>6</sup>, R<sup>7</sup>, R<sup>6a</sup> and R<sup>7a</sup> are independently selected at each occurrence from:

-H,  
-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> alkynyl, C<sub>1</sub>-C<sub>10</sub> haloalkyl with 1-10 halogens, C<sub>2</sub>-C<sub>8</sub> alkoxyalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, C<sub>5</sub>-C<sub>10</sub> cycloalkenyl, or C<sub>6</sub>-C<sub>14</sub> cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>13</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>13</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>13</sup>, NR<sup>16</sup>R<sup>15</sup>, CONR<sup>16</sup>R<sup>15</sup>, aryl, heteroaryl or heterocyclyl,  
-aryl, aryl(C<sub>1</sub>-C<sub>4</sub> alkyl), heteroaryl, heteroaryl(C<sub>1</sub>-C<sub>4</sub> alkyl), heterocyclyl or heterocyclyl(C<sub>1</sub>-C<sub>4</sub> alkyl);

alternatively, NR<sup>6</sup>R<sup>7</sup> and NR<sup>6a</sup>R<sup>7a</sup> are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C<sub>1</sub>-C<sub>4</sub> alkyl groups;

*contd.*  
*B1*  
R<sup>8</sup> is independently selected at each occurrence from H or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>9</sup> and R<sup>10</sup> are independently selected at each occurrence from H, C<sub>1</sub>-C<sub>4</sub> alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>11</sup> is selected from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>12</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> haloalkyl;

R<sup>13</sup> is selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>2</sub>-C<sub>8</sub> alkoxyalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>4</sub> alkyl)-, heteroaryl or heteroaryl(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

R<sup>14</sup> is selected from C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, or C<sub>4</sub>-C<sub>12</sub> cycloalkylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>15</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>15</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>15</sup>, NR<sup>16</sup>R<sup>15</sup>, CONR<sup>16</sup>R<sup>15</sup>, and C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>1</sub>-C<sub>6</sub> alkylsulfinyl and C<sub>1</sub>-C<sub>6</sub> alkylsulfonyl;

R<sup>15</sup> and R<sup>16</sup> are independently selected at each occurrence from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>4</sub>-C<sub>16</sub> cycloalkylalkyl, except that for S(O)<sub>n</sub>R<sup>15</sup>, R<sup>15</sup> cannot be H;

aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>15</sup>, COR<sup>15</sup>, CO<sub>2</sub>R<sup>15</sup>, OC(O)R<sup>15</sup>, NR<sup>8</sup>COR<sup>15</sup>, N(COR<sup>15</sup>)<sub>2</sub>, NR<sup>8</sup>CONR<sup>16</sup>R<sup>15</sup>, NR<sup>8</sup>CO<sub>2</sub>R<sup>15</sup>, NR<sup>16</sup>R<sup>15</sup>, and CONR<sup>16</sup>R<sup>15</sup>;

heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, halo, C<sub>1</sub>-C<sub>4</sub> haloalkyl, cyano, OR<sup>15</sup>, SH, S(O)<sub>n</sub>R<sup>15</sup>, -COR<sup>15</sup>,

$\text{CO}_2\text{R}^{15}$ ,  $\text{OC}(\text{O})\text{R}^{15}$ ,  $\text{NR}^8\text{COR}^{15}$ ,  $\text{N}(\text{COR}^{15})_2$ ,  $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$ ,  $\text{NR}^8\text{CO}_2\text{R}^{15}$ ,  $\text{NR}^{16}\text{R}^{15}$ , and  $\text{CONR}^{16}\text{R}^{15}$ ;

heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl, halo,  $\text{C}_1$ - $\text{C}_4$  haloalkyl, cyano,  $\text{OR}^{15}$ ,  $\text{SH}$ ,  $\text{S}(\text{O})_n\text{R}^{15}$ ,  $\text{COR}^{15}$ ,  $\text{CO}_2\text{R}^{15}$ ,  $\text{OC}(\text{O})\text{R}^{15}$ ,  $\text{NR}^8\text{COR}^{15}$ ,  $\text{N}(\text{COR}^{15})_2$ ,  $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$ ,  $\text{NR}^8\text{CO}_2\text{R}^{15}$ ,  $\text{NR}^{15}\text{R}^{16}$ , and  $\text{CONR}^{16}\text{R}^{15}$ ; and

n is independently at each occurrence 0, 1 or 2.

### REMARKS

Reconsideration of the present application is respectfully requested in view of the amendment to the claims and the following comments.

Claims 1, 2, 37 and 38 are pending in the application. Claim 1 has been amended to clarify the definition for the  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^{6a}$ , and  $\text{R}^{7a}$  substituents. This definition has not been substantively amended, but merely re-typed for purposes of clarification.

Claims 1, 2, 37 and 38 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that the re-typed definition for the  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^{6a}$ , and  $\text{R}^{7a}$  substituents in Claim 1 clarifies that no text was omitted, and that the claims are thus not indefinite. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 1, 2, 37 and 38 also stand rejected under 35 U.S.C. § 112, first paragraph, because Claim 1 does not include certain provisos that are set forth on pages 25 to 26 of the specification. Accordingly, the Examiner has asserted that Claim 1, without the provisos, is not supported in the specification. Applicants respectfully traverse this rejection.

Applicants respectfully submit that Claim 1, as currently pending is fully supported by the specification, for example, at pages 14 to 20. Applicants note that the genus of